

What is claimed is:

1 1. An apparatus for combinatorial chemistry on a
2 substrate comprising:

3 a manifold having one or more outlets positioned to
4 deliver one or more chemicals to the substrate; and

5 a linear drive for moving the substrate below the
6 manifold.

1 2. The apparatus of claim 1, wherein the manifold is
2 defined further as comprising one or more outlets that form
3 linear delivery spray heads.

1 3. The apparatus of claim 1, wherein the manifold
2 delivers one or more chemicals for nucleic acid synthesis to
3 the substrate.

1 4. The apparatus of claim 1, wherein the manifold
2 delivers one or more chemicals for peptide synthesis.

1 5. The apparatus of claim 1, wherein the manifold
2 delivers one or more chemicals for nucleic acid synthesis.

1 6. The apparatus of claim 1, wherein the manifold
2 delivers one or more chemicals for oligomer synthesis.

1 7. The apparatus of claim 1, wherein the manifold is
2 further defined as one or more manifolds comprising:

3 an acetonitrile manifold;

4 an oxidizer manifold;

5 a capping reagent manifold;

6 one or more monomer manifolds; and

7 a deblock manifold.

1 8. The apparatus of claim 1, further comprising a mask
2 containing one or more holes positioned between the manifold
3 and the substrate.

1 9. The apparatus of claim 1, wherein the substrate
2 comprises a chemically nonreactive material.

1 10. The apparatus of claim 1, wherein the substrate
2 comprises Delrin.

1 11. The apparatus of claim 1, wherein the substrate
2 comprises Polyethylene.

1 12. The apparatus of claim 1, wherein the substrate
2 comprises Fiberglass.

1 13. The apparatus of claim 1, wherein the substrate
2 comprises Glass Micro-fiber filter (GMFF).

1 14. The apparatus of claim 1, wherein the substrate
2 comprises a material coated with a chemically non-reactive
3 coating.

1 15. The apparatus of claim 1, wherein the substrate
2 comprises a top surface and wherein the top surface is
3 slanted.

1 16. The apparatus of claim 1, wherein the substrate
2 comprises one or more wells.

1 17. The apparatus of claim 1, wherein the substrate
2 comprises a multi-well plate.

1 18. The apparatus of claim 1, wherein the substrate
2 comprises a multi-well filter plate.

1 19. The apparatus of claim 16, wherein the one or more
2 wells of the plate further comprise a slanted interior edge.

1 20. The apparatus of claim 16, wherein the plate is
2 further define as a multi-well filter plate and comprises:

3 a top and a bottom plate containing one or more wells;
4 and

5 a semi-permeable membrane positioned between the top and
6 bottom plates.

1 21. The apparatus of claim 16, wherein the wells
2 comprise a slanted cross-section.

1 22. The apparatus of claim 16, wherein the wells
2 comprise a slanted cross-section and a frit.

1 23. The apparatus of claim 16, wherein the wells
2 comprise first and second slanted portions.

1 24. The apparatus of claim 16, wherein the wells
2 comprise first and second slanted portion, and wherein at
3 least one frit is fixed within the first or second slanted
4 portion of the well.

1 25. The apparatus as in claim 16, wherein each of the
2 one or more wells further comprise a synthesis substrate.

1 26. The apparatus of claim 1, further comprising a
2 computer connected to and controlling the linear drive.

1 27. The apparatus of claim 1, further comprising one or
2 more chemical reservoirs in fluid communication with one or
3 more manifolds.

1 28. The apparatus of claim 1, further comprising a
2 computer connected to and controlling one or more valves that
3 control the flow of fluid between the one or more chemical
4 reservoirs with the one or more manifolds.

1 29. The apparatus of claim 1, further comprising:

2 one or more chemical reservoirs in fluid communication
3 with the one or more manifolds; and

4 one or more valves control the flow of fluid from the
5 chemical reservoirs to the one or more manifolds.

1 30. The apparatus of claim 1, further comprising a mask
2 positioned between the manifold and the substrate.

1 31. The apparatus of claim 30, wherein the mask
2 positioned between the manifold and the substrate is layered
3 on the substrate.

1 32. The apparatus of claim 30, wherein a mask is
2 positioned further comprises one or more through-holes
3 generally over one or more reaction sites of the substrate.

1 33. The apparatus of claim 30, wherein the mask
2 comprises Teflon™.

1 34. The apparatus of claim 30, wherein the mask
2 comprises Teflon™ between 0.002 and 0.25 inches thick.

1 35. The apparatus of claim 30, wherein the mask
2 comprises polyethylene.

1 36. The apparatus of claim 30, wherein the mask
2 comprises fiberglass.

1 37. The apparatus of claim 30, wherein the mask
2 comprises Delrin.

1 38. The apparatus of claim 30, wherein the mask
2 comprises polypropylene.

1 39. The apparatus of claim 30, wherein the mask
2 comprises single-sided Teflon™ tape.

1 40. The apparatus of claim 30, wherein the mask
2 comprises molded polypropylene and further comprising divots
3 that generally match one or more wells of a substrate.

1 41. The apparatus of claim 30, wherein the mask
2 comprises molded polyethylene and further comprising divots
3 that generally match one or more wells of a substrate.

1 42. The apparatus of claim 30, wherein the mask
2 comprises a magnetically attractive material.

1 43. The apparatus of claim 30, wherein the mask
2 comprises an electrostatic charge opposite an electrostatic
3 charge on the substrate.

1 44. The apparatus of claim 1, further comprising a
2 vacuum in communication with the substrate.

1 45. The apparatus as in claim 1, wherein the substrate
2 comprises one or more reactive group protected from a chemical
3 reaction by one or more removable protecting groups.

1 46. The apparatus of claim 45, wherein the one or more
2 removable protecting groups is removed by addition of a
3 deblocking reagent.

1 47. The apparatus of claim 45, wherein the substrate
2 comprises one or more monomers for nucleic acid synthesis.

1 48. The apparatus of claim 45, wherein the substrate
2 comprises one or more monomers for peptide synthesis.

1 49. The apparatus of claim 45, wherein the substrate
2 comprises one or more monomers for peptide nucleic acid
3 synthesis.

1 50. The apparatus of claim 45, wherein the substrate
2 comprises one or more monomers for carbohydrate synthesis.

1 51. The apparatus of claim 45, wherein the substrate
2 further comprises a linker.

1 52. The apparatus of claim 45, wherein the substrate
2 comprises a small molecule library.

1 53. The apparatus of claim 1, wherein the substrate
2 comprises 6, 12, 48, 96, 384, 864, 1,536 or more reaction
3 sites.

1 54. The apparatus of claim 1, wherein the substrate is
2 rectangular.

1 55. The apparatus as in claim 1, wherein substrate
2 comprises one or more wells, and the one or more wells are
3 canted.

1 56. An apparatus for combinatorial chemistry comprising:
2 a substrate comprising one or more reaction sites;
3 a mask positioned on the substrate;
4 a one or more manifolds positioned to deliver one or more
5 chemicals to at least a portion of the substrate; and
6 a linear drive for moving the substrate and the mask
7 below the one or more linear manifolds.

1 57. An apparatus for combinatorial chemistry comprising:
2 a substrate comprising one or more reaction sites;
3 a mask comprising one or more through holes positioned
4 generally over the one or more reaction sites of the
5 substrate;
6 a one or more linear manifolds positioned to deliver one
7 or more chemicals to the substrate;

8 a linear drive for moving the substrate and the mask
9 below the one or more linear manifolds; and

10 a vacuum below the one or more reaction sites of the
11 substrate.

1 58. An apparatus for synthesizing oligomers comprising:

2 a substrate comprising one or more reaction sites;

3 a mask comprising one or more through holes positioned
4 generally over the one or more reaction sites of the
5 substrate;

6 one or more linear manifolds positioned to deliver one or
7 more chemicals to the substrate comprising:

8 an acetonitrile manifold;

9 an oxidizer manifold;

10 a capping reagent manifold;

11 one or more monomer manifold; and

12 a deblock manifold;

13 a linear motion table that moves the substrate and the
14 mask below the one or more manifolds; and

15 a vacuum below the one or more reaction sites of the
16 substrate.

1 59. A method for controlling a chemical reaction in one
2 or more reaction sites protected by a mask comprising the
3 steps of:

4 positioning a mask comprising one or more wells over a
5 substrate comprising one or more reaction sites;

6 flooding a deblock reagent over the surface of the mask,
7 wherein the deblock reagent will only enter unmasked reaction
8 sites;

9 removing the mask;

10 flooding a mix of activator and one reactive monomer into
11 all reaction sites;

12 flooding a mix of cap A and B reagents into all reaction
13 sites;

14 flooding and oxidizing reagent into all reaction sites;
15 and

16 repeating the above steps for the other reactive
17 monomers.

1 60. A method for controlling a chemical reaction in one
2 or more reaction sites protected by a mask comprising the
3 steps of:

4 (a) flooding a deblock reagent into all the reaction
5 sites of a substrate;

6 (b) positioning a monomer-specific mask for a specific
7 monomer over a substrate;

8 (c) flood a specific monomer and activator over the
9 substrate, wherein only those reaction sites with open holes
10 in the mask will receive one or more specific monomers;

11 (d) removing the mask; and

12 (e) repeating steps (b) through (d) for each specific
13 monomer;

14 (f) flooding a mix of cap A and B reagents into all
15 reaction sites; and

16 (g) flooding an oxidizing reagent into all reaction
17 sites.

1 61. A mask for chemical synthesis comprising:
2 a non-reactive sheet having a top and a bottom surface;
3 one or more through-holes that form an array that
4 generally match the position of one or more wells of a
5 substrate.

1 62. The mask of claim 61, wherein the substrate
2 comprises a multi-well plate.

1 63. The mask of claim 61, wherein the substrate
2 comprises a multi-well filter plate.

1 64. The mask of claim 61, wherein the mask comprises a
2 substantially chemically non-reactive material.

1 65. The mask of claim 61, wherein the mask comprises a
2 Teflon™-coated polymer.

1 66. The mask of claim 61, wherein the mask comprises
2 polyethylene.

1 67. The mask of claim 61, wherein the mask comprises
2 fiberglass.

1 68. The mask of claim 61, wherein the mask comprises
2 Delrin.

1 69. The mask of claim 61, wherein the mask comprises
2 polypropylene.

1 70. The mask of claim 61, wherein the through-holes are
2 further defined as having one or more nozzles on the bottom
3 surface.

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1 71. The mask of claim 70, wherein the through-holes are
2 further defined as having one or more nozzles on the bottom
3 surface, wherein the nozzles have an angle that matches the
4 angle of the wells in the multi-well plate.

1 72. The mask of claim 70, wherein the through-holes are
2 further defined as having one or more nozzles on the bottom
3 surface, wherein the nozzles have an angle that is more than
4 the angle of the wells in the multi-well plate.

1 73. The mask of claim 70, wherein the through-holes are
2 further defined as having one or more nozzles on the bottom
3 surface, wherein the nozzles have an angle that is less than
4 the angle of the wells in the multi-well plate.

1 74. A method of determining synthetic order of monomer
2 addition comprising the steps of:

3 determining the synthesis order for the addition of a
4 specific monomer;

5 deciding whether a mask is to be positioned on a
6 substrate;

7 moving the substrate to a preselected position for
8 chemical addition;

9 adding a specific monomer;

10 washing the substrate; and

11 repeating the above steps if another monomer is to be
12 added.

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1 75. The method of claim 74, wherein the step of
2 catalyzing the addition of a monomer is defined further as
3 comprising the steps of:

4 performing a deblock step;

5 putting on a mask to protect sites in which a monomer
6 will not be added;

7 delivering one or more monomers;

8 performing a capping steps and performing an oxidizer
9 step.

1 76. A method for producing polymers comprising the steps
2 of:

3 placing a reactive compound on one or more reaction sites
4 of a substrate;

5 protecting one or more reaction sites of a substrate with
6 a mask; and

7 controlling a chemical reaction in the one or more
8 reaction sites not protected by the mask.

1 77. The method of claim 76, wherein the step of
2 controlling a reaction is defined further as not deblocking
3 the reactive compound .

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1 78. The method of claim 76, wherein the step of
2 controlling a chemical reaction comprises the steps of:

3 flooding a deblocking reagent over the surface of the
4 mask;

5 flooding a coupling reagent over the surface of the mask,
6 wherein the coupling reagent comprises one or more reactive
7 compounds;

8 flooding a capping reagent over the surface of the mask;
9 and

10 flooding oxidizing reagent over the surface of the mask.

1 79. The method of claim 76, wherein the one or more
2 reactive compounds are defined further as phosphoramidite
3 comprising compounds.

1 80. The method of claim 76, wherein phosphoramidite
2 comprising compounds include one or more protected
3 phosphoramidite nucleic acid bases A, G, C, T, U or
4 derivatives thereof.

1 81. The method of claim 76, wherein chemical reaction is
2 the addition of one or more monomers for carbohydrate
3 synthesis.

1 82. The method of claim 76, wherein chemical reaction is
2 the addition of one or more monomers for nucleic acid
3 synthesis.

1 83. The method of claim 76, wherein chemical reaction is
2 the addition of one or more monomers for peptide synthesis.

1 84. The method of claim 76, wherein the capping agent
2 further comprises a cap A and a cap B reagent and wherein they
3 acetylate unreacted termini.

1 85. A method of determining the mask pattern for monomer
2 addition comprising the steps of:

3 reading the sequence of one or more monomer sequences;

4 setting up an array that contains all the possible
5 permutations of the monomers wherein each of these
6 permutations having a first and a second element, wherein the
7 first element records the number of cycles required to
8 complete synthesis and the second element records the number
9 of monomers to be deblocked;

10 selecting a variable number that equals the total number
11 of required monomers types;

12 selecting a second variable that contains the total
13 number of wells; and

14 testing the array for the minimum number of masks that
15 are required to complete all the monomer additions; and

16 selecting the array that contains the minimum number of
17 masks.

1 86. The method of claim 85, further comprising the step
2 of pre-determining areas with sequences in common within the
3 sequences of the one of more monomers and preparing masks for
4 those areas of with sequences in common independent from the
5 determination of the array.